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LAW OFFICES OF TRAVIS L. DODD
A PROFESSIONAL CORPORATION
2490 HEYNEMAN HOLLOW
FALLBROOK, CA 92028

EXAMINER	
TRAN, MY CHAU T	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 12/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/848,727	GAU, VINCENT JEN-JR.	
	Examiner	Art Unit	
	MY-CHAU T. TRAN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *83-95,98-104,108,112-118 and 120-127* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *83-95,98-104,108 and 112-127* is/are rejected.

7)☒ Claim(s) *123* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application and Claims Status

1. Applicant's amendment and response filed 09/12/2005 is acknowledged and entered. Claim 119 has been cancelled. Claims 83 and 120 have been amended. Claims 124-127 have been added. ***Furthermore***, the amendment filed includes claim(s) with improper status identifiers. See 37 CFR 1.121 and MPEP § 714. For examples, claim 108 is identified as "Currently Amended" yet ***no marking(s)*** to indicate the changes is present. Appropriate correction is required.

2. The amendment filed on 12/17/2004: cancelled claims 96, 97, 105-107, and 109-111; amended claims 83-86, 95, 98, 102-104, 108, and 112; and added claims 114-123.

3. The amendment filed on 06/28/2004: cancelled claims 1-20, 51-52, and 75-82; and added claims 83-113.

4. The amendment filed on 11/13/2003: cancelled claims 75-82; and added claims 75-82.

5. The amendment filed on 05/05/2003: cancelled claims 21-50; amended claims 1, 3-20; and added claims 51-74.

6. Claims 83-95, 98-104, 108, 112-118, 120-127 are pending.

Priority

7. This instant application claims benefit to a provisional application of 60/201,603 filed 05/03/2000. This instant application is granted the benefit of priority for 60/201,603 under 35 U.S.C 119(e).

8. Claims 83-95, 98-104, 108, 112-118, 120-127 are under consideration in this Office Action.

Maintained Rejection(s)

Claim Objections

9. Claim 123 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claim limitation of claim 123, i.e. "*employing the potential to determine the presence or quantity of the target analyte in the sample*", is similar to the limitation of claim 83, i.e. "*employing the measured current to determine the presence or quantity of a target analyte in the sample*". Thus, claim 123 is objected to as being of improper dependent form for failing to further limit the subject matter of a previous claim 83.

Claim Rejections - 35 USC § 102

10. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

11. Claims 83, 85-90, 94, 98-101, 103, 108, 112-118, 120, and 123-125 are rejected under 35 U.S.C. 102(e) as being anticipated by Choong et al. (US Patent 6,518,024). *Note: Claim 119 is cancelled and the limitation of claim 119 is added into claim 83.*

Choong et al. disclose an apparatus and methods for detecting single base extension to an oligonucleotide using electrochemical redox labels (see e.g. Abstract; col. 1, lines 7-16; col. 3, lines 25-31; col. 9, lines 17-22). The apparatus comprises a supporting substrate, a plurality of first electrodes (refers to instant claimed working electrode) in contact with the supporting substrate, a plurality of conjugated polymer (refers to claims 119 and 120) in contact with the plurality of first electrode wherein probes are immobilized, a counter electrode, and a reference electrode (see e.g. col. 5, line 15 thru col. 6, line 41; col. 7, lines 30-40). The substrate comprises materials such as silicon, glass, plastic, and ceramic (refers to instant claim 87) (see e.g. col. 5, lines 54-58). The first electrode comprises materials such as gold, titanium, and platinum (refers to claims 89, 90, 101, and 118) (see e.g. col. 5, line 59 thru col. 6, line 3). The counter electrode comprises materials such as gold, titanium, and platinum (refers to claims 89, 90, 101, and 118) (see e.g. col. 5, line 59 thru col. 6, line 3; col. 7, lines 29-40). The reference electrode comprises materials such as silver wire refers to instant claimed limitation of "*the reference electrode consists of a single layer of an electrically conductive material*", and claims 101 and 118). Additionally, the electrodes are connected to a power source and a means for controlling the power source. The substrate has a surface area of between 0.01 μm^2 and 5 cm^2 (refers to instant claim 113) (see e.g. col. 6, lines 12-26). The detection method includes amperometric and cyclic voltammetry (refers to instant claims 114-117) (see e.g. col. 4, lines 5-14; col. 10, lines 10-41).

The method comprises a) contacting the sample to the plurality of first electrodes, b) adding the reagent comprising the electrochemical redox labels, c) detecting the presence of the electrochemical redox labels to identify the base extension (see e.g. col. 4, lines 39-53; col. 8, lines 9-35; col. 10, lines 10-41). The detection step includes controlling the current flow between two electrodes (see e.g. col. 7, lines 41-50; col. 17-30). Thus, the apparatus and method of Choong et al. anticipated the presently claimed invention.

Additionally with regard to the newly added claims 124 and 125, Choong et al. disclose the step of forming the self-assembly monolayer on a working electrode (see e.g. col. 11, lines 31-40).

New Rejection(s) – Necessitated by Amendment

12. *The instant invention recites the method of detecting the presence or measuring the quantity of a target analyte in a sample reagent. The method comprises the step of 1) positioning the sample on a sensor; 2) conducting an analysis of the sample that includes controlling a potential difference between the reference electrode and the working electrode while measuring a current flowing through the working electrode wherein the potential is controlled so as to cause a redox reaction between a component in the sample and the working electrode, and the current through the working electrode is balanced by a current through the counter electrode; and 3) employing the measured current to determine the presence or quantity of a target analyte in the sample.*

The sensor structurally comprises a working electrode, a reference electrode, and a counter electrode on a substrate, and a self-assembly monolayer on at least one of the electrodes. The reference electrode structurally consists of a single layer of an electrically conductive material.

The method step of conducting an analysis is interpreted as controlling the potential difference between the counter electrode and the working electrode.

Claim Rejections - 35 USC § 112

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 124, 125, and 127 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) The method step limitation of "*forming the self-assembly monolayer on at least one of the electrodes*" of claim 124 is vague and indefinite because there is no correlation between this limitation and the presently claimed method steps of instant claim 83. The method of instant claim 83 recites "*the method of detecting the presence or measuring the quantity of a target analyte in a sample reagent*". The method comprises the step of 1) positioning the sample on a sensor; 2) conducting an analysis of the sample that includes controlling a potential difference between the reference electrode and the working electrode while measuring a current flowing through the working electrode wherein the potential is controlled so as to cause a redox reaction between a component in the sample and the working electrode, and the current through the working electrode is balanced by a current through the counter electrode; and 3) employing the measured current to determine the presence or quantity of a target analyte in the sample. The presently claimed method steps would result in detecting the target analyte in the sample, i.e. '*employing the measured current to determine the presence or quantity of a target analyte in the sample*', which does not correlates with the limitation of "*forming the self-assembly monolayer on at least one of the electrodes*" of claim 124. Thus, claim 124 is rejected under 35 U.S.C. 112, second paragraph.

b) The method step limitation of "*forming the self-assembly monolayer on the working electrode*" of claim 125 is vague and indefinite because there is no correlation between this limitation and the presently claimed method steps of instant claim 83. The method of instant

claim 83 recites "*the method of detecting the presence or measuring the quantity of a target analyte in a sample reagent*". The method comprises the step of 1) positioning the sample on a sensor; 2) conducting an analysis of the sample that includes controlling a potential difference between the reference electrode and the working electrode while measuring a current flowing through the working electrode wherein the potential is controlled so as to cause a redox reaction between a component in the sample and the working electrode, and the current through the working electrode is balanced by a current through the counter electrode; and 3) employing the measured current to determine the presence or quantity of a target analyte in the sample. The presently claimed method steps would result in detecting the target analyte in the sample, i.e. '*employing the measured current to determine the presence or quantity of a target analyte in the sample*', which does not correlates with the limitation of "*forming the self-assembly monolayer on the working electrode*" of claim 125. Thus, claim 125 is rejected under 35 U.S.C. 112, second paragraph.

c) The method step limitation of "*forming the self-assembly monolayer on the working electrode, counter electrode, and the reference electrode*" of claim 127 is vague and indefinite because there is no correlation between this limitation and the presently claimed method steps of instant claim 83. The method of instant claim 83 recites "*the method of detecting the presence or measuring the quantity of a target analyte in a sample reagent*". The method comprises the step of 1) positioning the sample on a sensor; 2) conducting an analysis of the sample that includes controlling a potential difference between the reference electrode and the working electrode while measuring a current flowing through the working electrode wherein the potential is controlled so as to cause a redox reaction between a component in the sample and the working

electrode, and the current through the working electrode is balanced by a current through the counter electrode; and 3) employing the measured current to determine the presence or quantity of a target analyte in the sample. The presently claimed method steps would result in detecting the target analyte in the sample, i.e. '*employing the measured current to determine the presence or quantity of a target analyte in the sample*', which does not correlates with the limitation of "*forming the self-assembly monolayer on the working electrode, counter electrode, and the reference electrode*" of claim 127. Thus, claim 1275 is rejected under 35 U.S.C. 112, second paragraph.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 83-91, 93, 94, 98-104, 112, 113, 115, 118, and 121-127 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weetall (US Patent 4,963,245) and Cozzette et al. (US Patent 5,200,051).

Weetall discloses a sensor apparatus for measuring the redox reaction occurring on the surface of the electrode array and the method for performing an immunoassay of an analyte on the sensor apparatus (see e.g. Abstract; col. 1, lines 8-12, and 46-68; claim 1).

The method comprises the steps of a) introducing into the well/sampling area the sample containing the analyte (refers to the instant claimed step (1)); b) applying a potential between the

working electrode and counter electrode (refers to instant claimed step (2)); c) measuring the current between the working electrode and counter electrode and determining the amount of analyte (refers to instant claimed step (2)); and d) determining the amount of the analyte in the test sample from the measurement of the current in step (c) relative to the preselected potential in step (b) (refers to the instant claimed step (3), and claim 123)(see e.g. col. 1, lines 53-55; col. 2, col. 3, line 18 to col. 4, line 33; claim 1).

The sensor apparatus comprises a planar support with a plurality of wells (refers to instant claim 93) or with out wells, i.e. with define sampling area (see e.g. col. 2, lines 45-51; figs 3 and 4); each well/sampling area comprises a working electrode, counter electrode, and reference electrode (refers to instant claimed working electrode, counter electrode, and reference electrode; and claim 112); and an ammeter to control and monitor the electrodes in the wells/sampling area (refers to instant claim 115)(see e.g. col. 1, lines 56-62; col. 2, lines 24-66; fig. 1-2, and 5; claim 1). Figures 3 and 4 disclose the arrangement of the electrodes on the support wherein the working electrode (ref. #22) is in the center and the counter electrode (ref. #26), and reference electrode (ref. # 24) are at the perimeter of the working electrode (refers to instant claims 99, 100, 121 and 122). The material for the support includes glass, and plastic polymer (refers to instant claim 87)(see e.g. col. 2, lines 26-29). The electrodes are graphite electrodes (refers to instant claimed limitation of "*the reference electrode consists of a single layer of an electrically conductive material*", and claims 101 and 118)(see e.g. col. 2, lines 38-42). The sample include biological sample and in liquid form (reefers to claims 85 and 86)(see e.g. col. 1, lines 63-68; col. 3, lines 4-13). Additionally, a sensor activating chemical attached to

the working electrode that include a first conjugate wherein it is a specific binding partner to the analyte of interest (refers to instant claim 98)(see e.g. col. 4, lines 55-60).

The apparatus of Weetall differs from the presently claimed invention by failing to disclose a self-assembly monolayer on at least one of the electrodes and an adhesive underneath each of the electrodes.

Cozzette et al. disclose a biosensor and various methods for using the biosensor (see e.g. Abstract; col. 1, lines 17-64; col. 11, line 49 to col. 12, line 25). In general, the method disclosed is the method of electrochemically detecting the changes in concentration of electroactive species that result from the reaction between the enzyme and the substrate with the biosensor (see e.g. col. 12, lines 7-25; col. 20, line 4 to col. 21, line 51; fig. 14). In general, the biosensor comprises a planar substrate and a base sensor that includes a unit cell that comprises an indicator electrode and a combined reference and counter electrode and an additional structure of a permaselective layer (see e.g. col. 12, lines 26-44; col. 24, lines 23-42; col. 26 line 36 thru col. 29, line 56; col. 56, lines 16-25; fig. 1, 4, and 12). The substrate comprises material such as silicon, glass, or plastic (see e.g. col. 24, lines 7-11; col. 25, lines 36-44). The electrode comprises material such as gold or platinum (e.g. col. 24, line 61 thru col. 25, line 8). A metal-substrate adhesive comprises a titanium layer (see e.g. col. 25, lines 55-61). The electrochemical detection means includes amperometric, potentiometric, or conductimetric (see e.g. col. 19, lines 31-35). Additionally, the unit cell is well in a microplate (see e.g. fig. 1, 4, and 12). One type of biosensor disclosed by Cozzette et al. is a glucose sensor and the method of detecting the concentration of the glucose in the sample by measuring the current generated as the result of the electrochemical reaction (see e.g. col. 22, lines 34-67; col. 23, lines 35-40; col. 43, lines 31-68).

The method comprises the step of applying the appropriate potential across the indicator electrode, with respect to the reference electrode, that result in the consumption of the electroactive species and the production of a measurable current (see e.g. col. 22, lines 34-67).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to disclose a self-assembly monolayer on at least one of the electrodes and an adhesive underneath each of the electrodes as taught by Cozzette et al. in the apparatus of Weetall. One of ordinary skill in the art would have been motivated to disclose a self-assembly monolayer on at least one of the electrodes and an adhesive underneath each of the electrodes in the apparatus of Weetall for the advantage of a) providing a layer that act as a barrier against interfering chemical species while allowing the transport of smaller detectable chemical moieties of transport (Cozzette: col. 12, lines 32-34) and b) providing an adhesive layer that promotes the adhesion the metal layer onto the substrate surface (Cozzette: col. 25, lines 58-61). And both Weetall and Cozzette et al. disclose a sensor and method of amperometric detection of glucose oxidation (Weetall: col. 2, lines 12-15; Cozzette: col. 22, lines 34-67). Furthermore, one of ordinary skill in the art would have a reasonable expectation of success in the combination of Weetall and Cozzette et al. because Cozzette et al. disclose the success via examples of a biosensor comprising a self-assembly monolayer and an adhesive layer underneath each of the electrodes (Cozzette: col. 68, line 40 thru col. 69, line 63).

Therefore, the combine teachings of Weetall and Cozzette et al. do render the method and apparatus of the instant claims *prima facie* obvious.

17. Claim 92 is rejected under 35 U.S.C. 103(a) as being unpatentable over Weetall (US Patent 4,963,245) and Cozzette et al. (US Patent 5,200,051) as applied to claims 83-91, 93, 94, 98-104, 112, 113, 115, 118, and 121-127 above in paragraph 16, and further in view of Buck, Jr. et al. (US Patent 6,294,062 B1; *filing date of 6/1/1998*).

Weetall discloses a sensor apparatus for measuring the redox reaction occurring on the surface of the electrode array and the method for performing an immunoassay of an analyte on the sensor apparatus (see e.g. Abstract; col. 1, lines 8-12, and 46-68; claim 1).

The method comprises the steps of a) introducing into the well/sampling area the sample containing the analyte (refers to the instant claimed step (1)); b) applying a potential between the working electrode and counter electrode (refers to instant claimed step (2)); c) measuring the current between the working electrode and counter electrode and determining the amount of analyte (refers to instant claimed step (2)); and d) determining the amount of the analyte in the test sample from the measurement of the current in step (c) relative to the preselected potential in step (b) (refers to the instant claimed step (3), and claim 123)(see e.g. col. 1, lines 53-55; col. 2, col. 3, line 18 to col. 4, line 33; claim 1).

The sensor apparatus comprises a planar support with a plurality of wells (refers to instant claim 93) or with out wells, i.e. with define sampling area (see e.g. col. 2, lines 45-51; figs 3 and 4); each well/sampling area comprises a working electrode, counter electrode, and reference electrode (refers to instant claimed working electrode, counter electrode, and reference electrode; and claim 112); and an ammeter to control and monitor the electrodes in the wells/sampling area (refers to instant claim 115)(see e.g. col. 1, lines 56-62; col. 2, lines 24-66; fig. 1-2, and 5; claim 1). Figures 3 and 4 disclose the arrangement of the electrodes on the

support wherein the working electrode (ref. #22) is in the center and the counter electrode (ref. #26), and reference electrode (ref. # 24) are at the perimeter of the working electrode (refers to instant claims 99, 100, 121 and 122). The material for the support includes glass, and plastic polymer (refers to instant claim 87)(see e.g. col. 2, lines 26-29). The electrodes are graphite electrodes (refers to instant claimed limitation of "*the reference electrode consists of a single layer of an electrically conductive material*", and claims 101 and 118)(see e.g. col. 2, lines 38-42). The sample include biological sample and in liquid form (reefers to claims 85 and 86)(see e.g. col. 1, lines 63-68; col. 3, lines 4-13). Additionally, a sensor activating chemical attached to the working electrode that include a first conjugate wherein it is a specific binding partner to the analyte of interest (refers to instant claim 98)(see e.g. col. 4, lines 55-60).

Cozzette et al. disclose a biosensor and various methods for using the biosensor (see e.g. Abstract; col. 1, lines 17-64; col. 11, line 49 to col. 12, line 25). In general, the method disclosed is the method of electrochemically detecting the changes in concentration of electroactive species that result from the reaction between the enzyme and the substrate with the biosensor (see e.g. col. 12, lines 7-25; col. 20, line 4 to col. 21, line 51; fig. 14). In general, the biosensor comprises a planar substrate and a base sensor that includes a unit cell that comprises an indicator electrode and a combined reference and counter electrode and an additional structure of a permaselective layer (see e.g. col. 12, lines 26-44; col. 24, lines 23-42; col. 26 line 36 thru col. 29, line 56; col. 56, lines 16-25; fig. 1, 4, and 12). The substrate comprises material such as silicon, glass, or plastic (see e.g. col. 24, lines 7-11; col. 25, lines 36-44). The electrode comprises material such as gold or platinum (e.g. col. 24, line 61 thru col. 25, line 8). A metal-substrate adhesive comprises a titanium layer (see e.g. col. 25, lines 55-61). The electrochemical detection means

includes amperometric, potentiometric, or conductimetric (see e.g. col. 19, lines 31-35). Additionally, the unit cell is well in a microplate (see e.g. fig. 1, 4, and 12). One type of biosensor disclosed by Cozzette et al. is a glucose sensor and the method of detecting the concentration of the glucose in the sample by measuring the current generated as the result of the electrochemical reaction (see e.g. col. 22, lines 34-67; col. 23, lines 35-40; col. 43, lines 31-68). The method comprises the step of applying the appropriate potential across the indicator electrode, with respect to the reference electrode, that result in the consumption of the electroactive species and the production of a measurable current (see e.g. col. 22, lines 34-67).

The combine teachings of Weetall and Cozzette et al. are obvious over the instant claimed method because one of ordinary skill in the art would have been motivated to disclose a self-assembly monolayer on at least one of the electrodes and an adhesive underneath each of the electrodes in the apparatus of Weetall for the advantage of a) providing a layer that act as a barrier against interfering chemical species while allowing the transport of smaller detectable chemical moieties of transport (Cozzette: col. 12, lines 32-34) and b) providing an adhesive layer that promotes the adhesion the metal layer onto the substrate surface (Cozzette: col. 25, lines 58-61). However, the combine teachings of Weetall and Cozzette et al. differ from the presently claimed invention by failing to include chromium as an adhesive.

Buck, Jr. et al. teaches immunosensors based on direct electrochemical measurement of detectable species with microarray electrodes under bipotentiostatic control and the method of detecting biological analytes in a liquid sample using the immunosensors (see e.g. Abstract; col. 1, lines 60-62; col. 3, lines 43-61; col. 4, lines 11-24). The method comprises the claimed step of 1) positioning the sample reagent on a biosensor (see e.g. col. 4, lines 27-31; col. 6, lines 49-53);

2) controlling a potential difference between two of the electrodes (see e.g. col. 4, lines 35-41; col. 6, lines 59-67; col. 7, lines 3-10); 3) measuring an electrical signal from the biosensor so as to determine the presence and/or quantity of the target analyte in the sample reagent (see e.g. col. 4, lines 41-50; col. 7, lines 1-2, and 11-15). The method of Buck, Jr. et al. further discloses the instant claimed method step of controlling the potential difference is between the reference electrode and the working electrode, and the application of the current is through the counter electrode (see e.g. col. 8, lines 51-61). The liquid sample is a biological fluid (see e.g. col. 7, lines 27-36). The immunosensors comprises the electrode structure that includes a reference electrode, working electrode and an auxiliary electrode for current control (see e.g. col. 43-61; col. 7, lines 65-66; col. 8, line 54-55). The electrode is on a silicon substrate with a layer of chromium, and comprise of gold (see e.g. col. 8, lines 26-40). The electrode structure is formed on an inner surface of a chamber for receiving the liquid sample (see e.g. col. 8, lines 41-45). The electrode structure also is in contact with conductors (see e.g. col. 49-50).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include chromium as an adhesive as taught by Buck, Jr. et al. in the combination of Weetall and Cozzette et al. One of ordinary skill in the art would have been motivated to include chromium as an adhesive in the combination of Weetall and Cozzette et al. for the advantage of providing an adhesive layer that promotes the adhesion the metal layer onto the substrate surface especially gold electrode on silicon surface (Buck, Jr.: col. 8, lines 26-40) since Weetall, Cozzette et al., and Buck, Jr. et al. disclose a biosensor and the method of measuring redox reaction (Weetall: col. 2, lines 12-15; Cozzette: col. 22, lines 34-67; Buck, Jr.: col. 3, lines 43-61). Furthermore, one of ordinary skill in the art would have a reasonable

expectation of success in the combination of Weetall, Cozzette et al., and Buck, Jr. because the type of adhesive use for the adhesion the metal layer onto the substrate surface would be a choice of experimental design and is considered within the purview of the cited prior art.

Therefore, the combine teachings of Weetall, Cozzette et al., and Buck, Jr. do render the method of the instant claims *prima facie* obvious.

18. Claim 95 is rejected under 35 U.S.C. 103(a) as being unpatentable over Weetall (US Patent 4,963,245) and Cozzette et al. (US Patent 5,200,051) as applied to claims 83-91, 93, 94, 98-104, 112, 113, 115, 118, and 121-127 above in paragraph 16, and further in view of Han et al. (US Patent 6,268,161 B1).

Weetall discloses a sensor apparatus for measuring the redox reaction occurring on the surface of the electrode array and the method for performing an immunoassay of an analyte on the sensor apparatus (see e.g. Abstract; col. 1, lines 8-12, and 46-68; claim 1).

The method comprises the steps of a) introducing into the well/sampling area the sample containing the analyte (refers to the instant claimed step (1)); b) applying a potential between the working electrode and counter electrode (refers to instant claimed step (2)); c) measuring the current between the working electrode and counter electrode and determining the amount of analyte (refers to instant claimed step (2)); and d) determining the amount of the analyte in the test sample from the measurement of the current in step (c) relative to the preselected potential in step (b) (refers to the instant claimed step (3), and claim 123)(see e.g. col. 1, lines 53-55; col. 2, col. 3, line 18 to col. 4, line 33; claim 1).

The sensor apparatus comprises a planar support with a plurality of wells (refers to instant claim 93) or with out wells, i.e. with define sampling area (see e.g. col. 2, lines 45-51; figs 3 and 4); each well/sampling area comprises a working electrode, counter electrode, and reference electrode (refers to instant claimed working electrode, counter electrode, and reference electrode; and claim 112); and an ammeter to control and monitor the electrodes in the wells/sampling area (refers to instant claim 115)(see e.g. col. 1, lines 56-62; col. 2, lines 24-66; fig. 1-2, and 5; claim 1). Figures 3 and 4 disclose the arrangement of the electrodes on the support wherein the working electrode (ref. #22) is in the center and the counter electrode (ref. #26), and reference electrode (ref. # 24) are at the perimeter of the working electrode (refers to instant claims 99, 100, 121 and 122). The material for the support includes glass, and plastic polymer (refers to instant claim 87)(see e.g. col. 2, lines 26-29). The electrodes are graphite electrodes (refers to instant claimed limitation of "*the reference electrode consists of a single layer of an electrically conductive material*", and claims 101 and 118)(see e.g. col. 2, lines 38-42). The sample include biological sample and in liquid form (reefers to claims 85 and 86)(see e.g. col. 1, lines 63-68; col. 3, lines 4-13). Additionally, a sensor activating chemical attached to the working electrode that include a first conjugate wherein it is a specific binding partner to the analyte of interest (refers to instant claim 98)(see e.g. col. 4, lines 55-60).

Cozzette et al. disclose a biosensor and various methods for using the biosensor (see e.g. Abstract; col. 1, lines 17-64; col. 11, line 49 to col. 12, line 25). In general, the method disclosed is the method of electrochemically detecting the changes in concentration of electroactive species that result from the reaction between the enzyme and the substrate with the biosensor (see e.g. col. 12, lines 7-25; col. 20, line 4 to col. 21, line 51; fig. 14). In general, the biosensor comprises

a planar substrate and a base sensor that includes a unit cell that comprises an indicator electrode and a combined reference and counter electrode and an additional structure of a permaselective layer (see e.g. col. 12, lines 26-44; col. 24, lines 23-42; col. 26 line 36 thru col. 29, line 56; col. 56, lines 16-25; fig. 1, 4, and 12). The substrate comprises material such as silicon, glass, or plastic (see e.g. col. 24, lines 7-11; col. 25, lines 36-44). The electrode comprises material such as gold or platinum (e.g. col. 24, line 61 thru col. 25, line 8). A metal-substrate adhesive comprises a titanium layer (see e.g. col. 25, lines 55-61). The electrochemical detection means includes amperometric, potentiometric, or conductimetric (see e.g. col. 19, lines 31-35). Additionally, the unit cell is well in a microplate (see e.g. fig. 1, 4, and 12). One type of biosensor disclosed by Cozzette et al. is a glucose sensor and the method of detecting the concentration of the glucose in the sample by measuring the current generated as the result of the electrochemical reaction (see e.g. col. 22, lines 34-67; col. 23, lines 35-40; col. 43, lines 31-68). The method comprises the step of applying the appropriate potential across the indicator electrode, with respect to the reference electrode, that result in the consumption of the electroactive species and the production of a measurable current (see e.g. col. 22, lines 34-67).

The combine teachings of Weetall and Cozzette et al. are obvious over the instant claimed method because one of ordinary skill in the art would have been motivated to disclose a self-assembly monolayer on at least one of the electrodes and an adhesive underneath each of the electrodes in the apparatus of Weetall for the advantage of a) providing a layer that act as a barrier against interfering chemical species while allowing the transport of smaller detectable chemical moieties of transport (Cozzette: col. 12, lines 32-34) and b) providing an adhesive layer that promotes the adhesion the metal layer onto the substrate surface (Cozzette: col. 25, lines 58-

61). However, the combine teachings of Weetall and Cozzette et al. differ from the presently claimed invention by failing to include the calibration step comprising using two different calibration solutions.

Han et al. disclosed a biosensor for measuring the concentration of organic molecules in a solution (see e.g. col. 1, lines 16-17). Han et al. claim a method of using the biosensor that included a calibration step (see e.g. col. 12, lines 33-35; col. 16, claim 20). The claim method step includes a control solution (calibration solution) and obtaining a signal. Additionally, the system can be recalibrated by using a calibration solution with unknown amount of analyte (see e.g. col. 12, lines 60-62).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the calibration step comprising using two different calibration solutions as taught by Han et al. in the combination of Weetall and Cozzette et al. One of ordinary skill in the art would have been motivated to include the calibration step comprising using two different calibration solutions in the combination of Weetall and Cozzette et al. for the advantage of determining the performance of the electrode before the analysis of the sample (Han: col. 12, lines 34-36) since Weetall, Cozzette et al., and Han et al. disclose a sensor and method of amperometric detection of glucose oxidation (Weetall: col. 2, lines 12-15; Cozzette: col. 22, lines 34-67; Han: col. 1, lines 16-21). Furthermore, one of ordinary skill in the art would have a reasonable expectation of success in the combination of Weetall, Cozzette et al., and Han et al. because the calibration step is necessary to ensure the working order of the electrode.

Therefore, the combine teachings of Weetall, Cozzette et al., and Han et al. do render the method of the instant claims *prima facie* obvious.

19. Claims 114, 116, and 117 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weetall (US Patent 4,963,245) and Cozzette et al. (US Patent 5,200,051) as applied to claims 83-91, 93, 94, 98-104, 112, 113, 115, 118, and 121-127 above in paragraph 16, and further in view of Glass et al. (US Patent 5,120,421).

Weetall discloses a sensor apparatus for measuring the redox reaction occurring on the surface of the electrode array and the method for performing an immunoassay of an analyte on the sensor apparatus (see e.g. Abstract; col. 1, lines 8-12, and 46-68; claim 1).

The method comprises the steps of a) introducing into the well/sampling area the sample containing the analyte (refers to the instant claimed step (1)); b) applying a potential between the working electrode and counter electrode (refers to instant claimed step (2)); c) measuring the current between the working electrode and counter electrode and determining the amount of analyte (refers to instant claimed step (2)); and d) determining the amount of the analyte in the test sample from the measurement of the current in step (c) relative to the preselected potential in step (b) (refers to the instant claimed step (3), and claim 123)(see e.g. col. 1, lines 53-55; col. 2, col. 3, line 18 to col. 4, line 33; claim 1).

The sensor apparatus comprises a planar support with a plurality of wells (refers to instant claim 93) or with out wells, i.e. with define sampling area (see e.g. col. 2, lines 45-51; figs 3 and 4); each well/sampling area comprises a working electrode, counter electrode, and reference electrode (refers to instant claimed working electrode, counter electrode, and reference electrode; and claim 112); and an ammeter to control and monitor the electrodes in the wells/sampling area (refers to instant claim 115)(see e.g. col. 1, lines 56-62; col. 2, lines 24-66; fig. 1-2, and 5; claim 1). Figures 3 and 4 disclose the arrangement of the electrodes on the

support wherein the working electrode (ref. #22) is in the center and the counter electrode (ref. #26), and reference electrode (ref. # 24) are at the perimeter of the working electrode (refers to instant claims 99, 100, 121 and 122). The material for the support includes glass, and plastic polymer (refers to instant claim 87)(see e.g. col. 2, lines 26-29). The electrodes are graphite electrodes (refers to instant claimed limitation of "*the reference electrode consists of a single layer of an electrically conductive material*", and claims 101 and 118)(see e.g. col. 2, lines 38-42). The sample include biological sample and in liquid form (reefers to claims 85 and 86)(see e.g. col. 1, lines 63-68; col. 3, lines 4-13). Additionally, a sensor activating chemical attached to the working electrode that include a first conjugate wherein it is a specific binding partner to the analyte of interest (refers to instant claim 98)(see e.g. col. 4, lines 55-60).

Cozzette et al. disclose a biosensor and various methods for using the biosensor (see e.g. Abstract; col. 1, lines 17-64; col. 11, line 49 to col. 12, line 25). In general, the method disclosed is the method of electrochemically detecting the changes in concentration of electroactive species that result from the reaction between the enzyme and the substrate with the biosensor (see e.g. col. 12, lines 7-25; col. 20, line 4 to col. 21, line 51; fig. 14). In general, the biosensor comprises a planar substrate and a base sensor that includes a unit cell that comprises an indicator electrode and a combined reference and counter electrode and an additional structure of a permaselective layer (see e.g. col. 12, lines 26-44; col. 24, lines 23-42; col. 26 line 36 thru col. 29, line 56; col. 56, lines 16-25; fig. 1, 4, and 12). The substrate comprises material such as silicon, glass, or plastic (see e.g. col. 24, lines 7-11; col. 25, lines 36-44). The electrode comprises material such as gold or platinum (e.g. col. 24, line 61 thru col. 25, line 8). A metal-substrate adhesive comprises a titanium layer (see e.g. col. 25, lines 55-61). The electrochemical detection means

includes amperometric, potentiometric, or conductimetric (see e.g. col. 19, lines 31-35). Additionally, the unit cell is well in a microplate (see e.g. fig. 1, 4, and 12). One type of biosensor disclosed by Cozzette et al. is a glucose sensor and the method of detecting the concentration of the glucose in the sample by measuring the current generated as the result of the electrochemical reaction (see e.g. col. 22, lines 34-67; col. 23, lines 35-40; col. 43, lines 31-68). The method comprises the step of applying the appropriate potential across the indicator electrode, with respect to the reference electrode, that result in the consumption of the electroactive species and the production of a measurable current (see e.g. col. 22, lines 34-67).

The combine teachings of Weetall and Cozzette et al. are obvious over the instant claimed method because one of ordinary skill in the art would have been motivated to disclose a self-assembly monolayer on at least one of the electrodes and an adhesive underneath each of the electrodes in the apparatus of Weetall for the advantage of a) providing a layer that act as a barrier against interfering chemical species while allowing the transport of smaller detectable chemical moieties of transport (Cozzette: col. 12, lines 32-34) and b) providing an adhesive layer that promotes the adhesion the metal layer onto the substrate surface (Cozzette: col. 25, lines 58-61). However, the combine teachings of Weetall and Cozzette et al. differ from the presently claimed invention by failing to disclose using cyclic voltammetry analysis.

Glass et al. disclose an electrochemical detection system and the method of making it (see e.g. Abstract; col. 1, 12-20; col. 3, lines 38-65; col. 4, lines 34-43). The electrochemical detection system comprises a plurality of electrodes on a flat wafer wherein the electrodes include a working electrode, an auxiliary electrode, and/or reference electrode (see e.g. col. 6, line 49 thru col. 7, line 10; col. 8, lines 3-47; col. 8, line 48 thru col. 9, line 2; col. 9, lines 30-45).

The type of material use for each electrode includes platinum and gold (see e.g. col. 8, lines 3-47; col. 14, line 48 thru col. 15, line 19). The wafer comprises of material such as silicon or ceramic (see e.g. col. 9, lines 10-20; col. 10, line 31-33; col. 14, lines 48-50). A layer of chromium or niobium is deposited on the wafer before deposit of the electrode material in order to increase the adhesion of the electrode material (see e.g. col. 10, lines 60-64; col. 14, lines 48-50). The system is equipped to perform cyclic voltammetry (see e.g. col. 5, lines 33-41).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to disclose using cyclic voltammetry analysis as taught by Glass et al. in the combination of Weetall and Cozzette et al. One of ordinary skill in the art would have been motivated to disclose using cyclic voltammetry analysis in the combination of Weetall and Cozzette et al. for the advantage of providing a detector has a high signal-to-noise ratio and improved selectivity (Glass: col. 4, lines 44-46) since Weetall, Cozzette et al., and Glass et al. disclose the method of using an electrochemical detection system for the detection of chemical compounds in solution (Weetall: col. 2, lines 12-15; Cozzette: col. 22, lines 34-67; Glass: col. 3, lines 54-58). Furthermore, one of ordinary skill in the art would have a reasonable expectation of success in the combination of Weetall, Cozzette et al., and Glass et al. because Glass et al. disclose the success of depositing a single layer of metal onto support by example (col. 14, line 48 thru col. 15, line 19).

Therefore, the combine teachings of Weetall, Cozzette et al., and Glass et al. do render the method of the instant claims *prima facie* obvious.

Withdrawn Objection(s) and/or Rejection(s)

20. The objection of claim 112 has been withdrawn in light of applicant's arguments, see pg. 7, filed 09/12/2005.

21. The rejections of claims 83-95, 98-101, 108, and 112-123 under 35 USC 112, second paragraph, as being indefinite have been withdrawn in light of applicant's arguments, see pg. 7-8, filed 09/12/2005.

22. The rejection of claims 83, 85-87, 93, 98, 99, 100, 101, 104, 112, 115, 118, and 121-123 under 35 USC 102(b) as being anticipated by Weetall (US Patent 4,963,245) has been withdrawn in light of applicant's amendment of claim 83.

23. The rejection of claims 83, 85-87, 93, 95, 98, 99, 100, 101, 104, 112, 115, 118, and 121-123 under 35 USC 103(a) as being obvious over Weetall (US Patent 4,963,245) and Han et al. (US Patent 6,268,161 B1) has been withdrawn in view of applicant's amendment of claim 83.

24. The rejection of claims 83-94, 99-101, 103, 108, 112, 114-118, and 123 under 35 USC 103(a) as being obvious over Buck, Jr. et al. (US Patent 6,294,062 B1; *filing date of 6/1/1998*) and Glass et al. (US Patent 5,120,421) has been withdrawn in view of applicant's amendments of claim 83.

Response to Arguments

25. Applicant's argument directed to the objection under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim for claim 123 have been fully considered but they are not persuasive for the following reasons.

Applicant contends that '*Claim 123 adds an element to Independent Claim 83*' because '*Claim 123 requires use of both current and potential where claim 83 requires only use of current*'. Thus, Claim 123 properly narrows Claim 83.

Applicant's arguments are not convincing since Claim 123 does not properly narrows Claim 83. The term "potential" as define by the Webster Diction as a unit charge, i.e. the term "potential" is synonymous with the term "current". This interpretation is further support by the definition of the term "potential" by the Electrochemistry Dictionary. Therefore, Claim 123 does not properly narrows Claim 83, and the rejection is maintained.

26. Applicant's argument directed to the rejection under 35 USC 102(e) as being anticipated by Choong et al. (US Patent 6,518,024) for claims 83, 85-90, 94, 98-101, 103, 108, 112-118, 120, and 123 (*Note: Claim 119 is cancelled and the limitation of claim 119 is added into claim 83*) was considered but they are not persuasive for the following reasons.

Applicant alleges that the device and method of Choong et al. do not anticipate the method of the instant claims because '*Choong does not teach a self-assembly monolayer positioned on at least one electrode of a sensor including a working electrode*'. Thus, the device and method of Choong et al. do not anticipate the method of the instant claims.

Applicant's arguments are not convincing since the teachings of Choong et al. do anticipate the method of the instant claims. It is the examiner position is that Choong et al. do disclose '*a self-assembly monolayer positioned on at least one electrode of a sensor including a working electrode*' (see e.g. col. 6, lines 30-32; col. 11, lines 31-40). Therefore, the teachings of Choong et al. do anticipate the method of the instant claims, and the rejection is maintained.

Conclusion

27. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 571-272-0810. The examiner can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct
December 1, 2005

PADMASHRI PONNALURI
PRIMARY EXAMINER